REMARKS

Amendments to Claims

Claims 1 and 4-7 have been amended. The Examiner rejected Claim 1 under 35 U.S.C. § 112, ¶ 2 because "there is not a step recited wherein the effect of the drug candidate on the target ion channel is detected." Claim 1 has been amended consistent with the Examiner's suggestion and to specify that the repetitive application of electric fields to set a transmembrane potential is applied with extracellular electrodes. Support in the Specification for amended Claim 1 is found, for example, on page 18 lines 15-20, page 21 line 20 – page 22 line 14, page 23 lines 11 – page 24 line 16.

The Examiner rejected Claims 4-6 under 35 U.S.C. § 112, ¶ 2 because "it is not clear whether 'an ion channel of interest' is the 'target ion channel' recited in [C]laim 1." Claims 4-6 have been amended to clarify any confusion by replacing "ion channel of interest" with "said target ion channel," which has an antecedent basis in Claim 1.

The Examiner rejected Claim 7 under 35 U.S.C. § 112, ¶ 2 because "the phrase 'said one or more cells' lack[ed] antecedent basis." Claim 7 has been amended to state "said plurality of host cells," which has an antecedent basis in Claim 1.

Rejection under 35 U.S.C. § 102(b)

Claims 1, 2 and 4-6 were rejected under 35 U.S.C. § 102(b) as being anticipated by *Catterall et al.* U.S. Pat. No. 5,437,982. *Catterall* does not anticipate amended Claims 1, 2 and 4-6.

Amended Claim 1 claims a method of screening a plurality of drug candidate compounds against a target ion channel comprising expressing said target ion channel in a population of host cells, placing a plurality of the host cells into each of a plurality of sample wells, adding a candidate drug compound to at least one of the plurality of sample wells and modulating a transmembrane potential of host cells in the plurality of sample wells with a repetitive application of electric fields applied with extracellular electrodes so as to set the transmembrane potential to a level corresponding to a pre-selected voltage dependent state of the target ion channel and detecting an effect of the candidate drug compound on the target ion channel.

Catterall does not teach "repetitive application of electric fields applied with extracellular electrodes so as to set said transmembrane potential to a level corresponding to a pre-selected voltage dependent state of said target ion channel." Instead, *Catterall* specifically teaches breaking through the cell membrane and inserting an electrode into a cell to directly manipulate the membrane potential. *See Catterall* at col. 3 lines 20-25. The method of *Catterall* requires access to both the internal and external portions of the cell membrane. It does not teach or suggest a manipulation of cell membrane potential to a specific level with extracellular electrodes. *Catterall* does not disclose "repetitive application of electric fields applied with extracellular electrodes so as to set said transmembrane potential to a level corresponding to a pre-selected voltage dependent state of said target ion channel." Thus, *Catterall* does not anticipate Claims 1, 2 and 4-6.

Rejections under 35 U.S.C. § 103(a)

Claims 1-6 were rejected under 35 U.S.C. § 103(a) as unpatentable over *Catterall* in view of *Tung et al.* (Biophysical Journal, 1992, 63(2): 371-386). The Examiner noted that although *Catterall* "does not expressly disclose repetitive application of biphasic electric fields", *Tung* "discloses comparison of the effects of biphasic and monophasic electric fields on the electrical stimulation of cardiac cells." Further, Claims 1, 2 and 4-7 were rejected under 35 U.S.C. § 103(a) as unpatentable over *Catterall* in view of *Tsien et al.* WO 96/41166 or *Denyer et al.* (Drug Discovery Today, 1998, 3(7): 323-332). The Examiner noted that although *Catterall* "does not expressly disclose a method wherein the host cells comprise a voltage sensor" *Tsien* "discloses a screening method for identifying drugs that affect ion channel activity corresponding to changes in membrane potentials in cells." The Examiner also noted that "Denyer et al. review high throughput screening (HTS) methods for voltage-gated ion channel modulators. Radiotracers, including radioactive ions, are noted for their use in tracing ion flux through ion channels . . . . Furthermore, high throughput methods have been established for enabling ion channel assays with radiotracers."

Claims 1-6 are not obvious. A *prima facie* case of obviousness requires that all of the claim limitations are taught or suggested by the prior art. *See* M.P.E.P. § 2143.03. The specific elements and limitations in Claim 1 are not disclosed by *Catterall*, *Tung*, *Denyer* or *Tsien*.

As noted above, *Catterall* does not disclose "repetitive application of electric fields applied with extracellular electrodes so as to set said transmembrane potential to a level corresponding to a pre-selected voltage dependent state of said target ion channel." *Tung*, *Tsien* and *Denyer* do not either. *Tung* discloses the electrical stimulation of cardiac cells through the use of a single pulse followed by a lag time to determine an excitation threshold. *Tung at 375.* *Tsien* stimulates a transmembrane electrical potential, not through electrical pulses, but through chemical stimulation. *See e.g., Tsien at 3.* *Denyer* likewise does not set transmembrane potentials to a preselected voltage state using repetitive electric fields. Instead, *Denyer* discloses ion channel assays with radiotracers. *See Denyer at 325-29.* Because *Catterall*, *Tung*, *Denyer* and *Tsien* do not disclsose a "repetitive application of electric fields applied with extracellular electrodes so as to set said transmembrane potential to a level corresponding to a pre-selected voltage dependent state of said target ion channel" their combination does not produce all of the elements of Claim 1. Thus, we respectfully request that the rejection of Claims 1-6 for obviousness be withdrawn.

CONCLUSION

The Applicants have endeavored to address all of the Examiner's concerns as expressed in the previous Office Action. Accordingly, amendments to the claims, the reasons therefor and arguments in support of the patentability of the pending claim set are presented above. In light of these amendments and remarks, reconsideration and withdrawal of the outstanding rejections is respectfully requested.

If any issues remain that could be resolved by telephone, the Examiner is invited to call the undersigned directly. Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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